Clinical-laboratory findings and risk factors in pulmonary embolism: A retrospective evaluation in the emergency service

Pulmonary embolism: A retrospective evaluation

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Abstract

Aim: The objective of this study is to retrospectively identify the demographic characteristics of patients diagnosed with pulmonary embolism in the emergency department, aiming to provide clinicians with new perspectives on the diagnosis of the disease. For this purpose, the clinical symptoms, risk factors, comorbid diseases, laboratory findings, and radiological results in those patients were detected.

Material and Methods: This single-center, retrospective, and observational study consisted of patients older than 18 years of age who presented to the emergency service with various complaints and were subsequently diagnosed with PE. Medical records, radiological results, and laboratory findings of the patients were documented for this research.

Results: A total of 37 cases were included in this study, with ages ranging from 25 to 89 (mean 66.24 ± 17.10). When evaluated based on the clinical symptoms, the most observed complaints were shortness of breath (n=24; 64.9%) and chest pain (n=16; 43.2%). The most frequently observed comorbidities were hypertension and diabetes, which were detected in 15 patients (40.5%) and 11 patients (29.7%), respectively.

Discussion: The findings of the present study revealed that in addition to typical clinical findings, PE may present with atypical symptoms that are not specific to the disease. In this context, the diagnosis of PE should not only be considered in the presence of typical symptoms but also taken into account when atypical symptoms that are not specific to PE exist.

Keywords

Emergency Department, Pulmonary Embolism, Comorbidity, Risk Factors, Clinical Symptoms

Introduction

Pulmonary embolism (PE), a remarkable disease highly associated with morbidity, is the third most common cause of in-hospital deaths after acute myocardial infarction and stroke [1]. Diagnosing PE is often challenging, and primarily suspicion of the disease is necessary before making the diagnosis [2]. Sudden-onset shortness of breath, chest pain, cyanosis, hemoptysis, and occasionally, pain accompanied by swelling in the legs are the most common symptoms of PE [1, 3].

Although previous studies have reported an increasing trend in annual PE incidence rates, current research draws attention to a significant decline in mortality rates attributed to PE [4]. The more frequent application of effective treatment methods is considered the main factor contributing to the observed positive changes in the prognosis of PE [5]. Due to the widespread use of advanced diagnostic methods, today clinically insignificant cases of PE that are not life-threatening are more frequently detected. This situation leads to an increase in the diagnosed cases of PE that consequently results in a relative decrease in mortality [6]. Another possible reason for the decrease in mortality rates in PE cases is that physicians working in emergency departments lately have been more frequently suspecting PE [7].

In previous studies regarding PE, it was suggested that approximately half of the PE patients admitted to the emergency department were not accurately diagnosed [8]. The difficulty in diagnosing PE arises from the fact that the disease can indicate classical symptoms such as shortness of breath and pleuritic chest pain, while it can also come up with atypical findings, such as syncope and slow-onset shortness of breath which are not characteristic of PE [9].

Diagnostic algorithms and techniques used in the diagnosis of PE have remained relatively unchanged in recent years, and the fundamental tool still employed for diagnosing the disease is computed tomography pulmonary angiography (CTPA) [10, 11]. In cases where clinical suspicion of PE is present, non-invasive diagnostic methods such as D-dimer blood test, clinical probability scoring, echocardiography, and serial ultrasonography of the legs are also utilized in addition to CTPA [4, 12]. This study aims to retrospectively identify the demographic characteristics of patients diagnosed with PE in the emergency department, aiming to provide clinicians with new perspectives in the diagnosis of the disease. The symptoms at the time of hospital admission, risk factors, comorbid diseases, laboratory findings, radiological results, risk classification scores, and prognoses in those patients were detected.

Material and Methods

Study Design: This single-center, retrospective, and observational study consisted of patients older than 18 years of age who presented to the Emergency Medicine Clinic of Bakırköy Dr. Sadi Konuk Training and Research Hospital with various complaints and symptoms between March 15, 2009, and March 15, 2011. Those patients were subsequently diagnosed with PE following advanced diagnostic investigations.

Study Protocol: To identify patients for inclusion in the study and to exclude those with incorrectly entered data, all patients for whom D-dimer analysis was requested were initially detected from laboratory records. The medical records and computed tomography (CT) findings of these identified patients were then reviewed for PE diagnosis. Following this examination, a total of 37 patients with confirmed PE diagnosis were included in the study.

Medical records, radiological results, and laboratory findings of the patients were documented in a research form prepared for this study. Hospital records of all patients were examined for clinical symptoms at the time of admission and the presence of risk factors for PE. In addition to demographic data, vital signs detected in the emergency department, existing comorbidities, electrocardiography (ECG) findings, radiological imaging results, blood gas analysis, troponin, and D-dimer values were recorded in the research form. In order to obtain data on the prognosis of the disease, the research form also included information concerning the duration of hospital stay, discharge details, and the treatment method applied. Furthermore, based on the available data, the Wells score was calculated for all patients.

Statistical Analysis: Statistical Package for the Social Sciences (SPSS) for Windows version 21.0 was used for the statistical analysis of the obtained data. Descriptive statistics such as mean, standard deviation, frequency, and ratio values were used for data that followed a normal distribution. The Kolmogorov-Smirnov test was utilized to assess the normality distribution of the parameters. Continuous variables were presented as mean ± standard deviation, whereas categorical values were expressed as absolute numbers and percentages.

Ethical Approval

This study was approved by the Ethics Committee of Bakırköy Dr. Sadi Konuk Training and Research Hospital (Date: 2011-04-18, No:2011/4-05).

Results

A total of 37 cases were included in this study, with ages ranging from 25 to 89 (mean 66.24 ± 17.10), including 22 females (59.5%) and 15 males (40.5%). Table 1 indicates clinical symptoms and signs of the cases of the patients presented at the emergency department. When evaluated based on the initial symptoms, shortness of breath (n=24; 64.9%) and chest pain (n=16; 43.2%) were the most observed complaints. In addition to these findings, pain or temperature change in the lower extremity (n=7, 18.9%), syncope (n=5; 13.5%), and confusion (n=4; 10.8%) were other frequently encountered symptoms. It is also noteworthy that non-specific symptoms such as headache (n=3; 8.1%), stomachache (n=3; 8.1%), lower back pain (n=2; 5.4%), dysuria (n=1; 2.7%), and speech disorder (n=1; 2.7%) were present in the patients included in the study. When evaluating the cases of PE in terms of risk factors, the most common ones identified were immobilization, swelling or temperature changes in one leg, recent history of surgery, or trauma (Table 2). The most frequently observed comorbidities, presented in Table 2, were hypertension and diabetes, which were detected in 15 patients (40.5%) and 11 patients (29.7%), respectively. In addition to these two pathologies, other diseases recorded were congestive heart failure, chronic obstructive pulmonary disease, coronary artery disease, and chronic kidney failure. No

malignancy was detected in any of the patients included in the study.

When electrocardiography (ECG) findings were assessed (Table 2), sinus tachycardia was detected in 12 patients (32.4%), while an S1Q3T3 pattern was observed in only 1 patient (2.7%).

Table 1. Clinical symptoms and signs of the cases at presentation

Symptom/Sign	Number of Patients (n)	Percentage
Dyspnea	24	64.9%
Chest pain	16	43.2%
Lower extremity pain/temperature change	7	18.9%
Syncope	5	13.5%
Confusion	4	10.8%
Fever	3	8.1%
Tachycardia	3	8.1%
Headache	3	8.1%
Stomachache	3	8.1%
Lower back pain	2	5.4%
Sore throat	1	2.7%
Dysuria	1	2.7%
Speech disorder	1	2.7%

Table 2. Characteristics of the cases submitted to the emergency department

		Number of Patients (n)	Percentage
Risk factors	Prolonged immobility	25	67.6%
	Recent surgery/trauma	9	24.3%
	Lower extremity pain/temperature change	7	18.9%
	Previous VTE/PE	6	16.2%
	Pregnancy	2	5.4%
	Use of oral contraceptives	1	2.7%
Comorbid diseases	Hypertension	15	40.5%
	Diabetes	11	29.7%
	Congestive heart failure	10	27%
	COPD	9	24.3%
	Ischemic heart disease	7	18.9%
	Chronic kidney disease	4	10.8%
	Malignancy	-	-
ECG findings	Sinus tachycardia	12	32.4%
	S1Q3T3 wave pattern	1	2.7%

VTE: Venous thromboembolism, PE: Pulmonary embolism, COPD: Chronic obstructive pulmonary disease, ECG: Electrocardiography.

Table 3. Laboratory findings of the cases submitted to the emergency department

		Mean ± SD	Cut-off range
Laboratory findings	D-dimer µg/L	6993.2 ± 7565.7	0-500
	Troponin ng/L	0.3 ± 0.6	0-0.4
	pH log [H+]-	7.4 ± 0.1	7.35-7.45
	pO2 mmHg	59.8 ±29.7	70-100
	pCO2 mmHg	38.3 ± 9.2	35-45
	HCO3 mEq/L	22.6 ± 4.6	22-28

SD: Standard deviation.

Laboratory findings of the patients can be seen in Table 3. Evaluating the patients in terms of these average laboratory data, the results were as follows: D-dimer 6993.2 ± 7565.7 µg/L (0-500), troponin 0.3 ± 0.6 ng/L (0-0.4), pH 7.4 ± 0.1 (7.35-7.45), pO2 59.8 ± 29.7 mmHg (70-100), pCO2 38.3 ± 9.2 mmHg (35-45), HCO3 22.6 ± 4.6 mEq/L (22-28).

Examining the hospital records of the patients, it was determined that hospitalization was conducted for 20 patients (54.1%), and thrombolytic therapy was administered to 5 of these patients (13.5%). It was observed that 15 of the patients (40.5%) were referred to another healthcare institution, and 2 patients (5.4%) unfortunately passed away.

All patients diagnosed with PE were assessed for the risk of venous thromboembolism (VTE) according to the Wells scoring system. The presence of high risk was identified in 12 patients (Wells score > 6; 32.4%), moderate risk was recorded in 25 patients (Wells score: 2-6; 67.6%), whereas no patients were identified with low risk (Wells score < 2; 0%).

Discussion

PE remains a prevalent and life-threatening disease that is still underdiagnosed in contemporary healthcare. The risk of PE significantly increases with increased age, given the rising incidence of VTE [2]. In fact, in the current study, the average age of the patients diagnosed with PE was determined to be 66.24 ± 17.10. Similarly, in a study conducted by Le Gal et al. [2] involving 416 patients diagnosed with PE, the average age was found to be 60.50 ± 19.10. In contrast to these results, another study conducted by Hacıevliyagil et al. [13] analyzed 63 patients diagnosed with PE, revealing an average age of 49.40 ± 16.80. When compared to the findings of the present study, it is evident that the average age in this research is considerably lower. The reason for this difference may be attributed to the potential impacts of other factors except for age on the incidence of PE such as environmental effects, genetic predisposition, and individual habits. Consequently, when making age-related correlations with PE, it is crucial to consider these highlighted factors.

The current study found that 59.5% of the patients diagnosed with PE were female, while 40.5% were male. Similar to our findings, two different research conducted by Pribish et al. [14] and Hacıevliyagil et al. [13] also reported higher proportions of females diagnosed with PE compared to males. On the other hand, in general, PE is more frequently observed in males than females across all races and age groups [3]. In this manner, the findings of the present study were in contrast to the literature. In high-income countries, the rate of women giving birth at age 35 and above has been recently increasing [15]. The widely preferred use of oral contraceptives for birth control among women of reproductive age is one of the most common risk factors for VTE [4]. However, not only in women of reproductive age but also in postmenopausal women receiving hormone replacement therapy, the risk of VTE is significantly increased [4]. Therefore, these factors could be considered as probable reasons for the contrary findings of literature obtained in the present study.

The most observed symptoms in patients diagnosed with PE include sudden-onset shortness of breath, pleuritic chest

pain, hemoptysis, cough, leg pain or swelling [1,4]. Similar symptoms were identified in the patients included in the current study where the most common symptoms upon emergency department admission were shortness of breath, chest pain, and pain or temperature change in the lower extremity. Despite not being the primary complaint, the presence of non-specific symptoms such as stomachache, dysuria, speech disorder, and lower back pain is noteworthy. Likewise, in the literature, some atypical symptoms such as diarrhea and loss of appetite [16], as well as dizziness [17] have been reported alongside the typical symptoms of PE. In this context, the diagnosis of PE should not only be considered in the presence of typical symptoms but also taken into account when atypical symptoms that are not specific to PE exist.

In the current study, hypertension and diabetes were found to be the highly observed comorbidities accompanying PE in the evaluated cases. In addition to the mentioned pathologies, congestive heart failure, chronic obstructive pulmonary disease, coronary artery disease, and chronic kidney disease were also identified, albeit with lower frequencies. Interestingly, unlike the literature, no cases of malignancy were observed in patients diagnosed with PE in the present study. Previously, comprehensive research conducted by Glise-Sandblad et al. [18] on 1.48 million patients identified malignancy (21.3%), congestive heart disease (18.3%), and ischemic heart disease (18.3%) as the most frequently associated diseases with PE. A different study by Ebner et al. [19] found that chronic kidney disease (34.2%), coronary artery disease (18.2%), and active malignancy (18.1%) were the most common comorbidities accompanying PE. In another study conducted by Huerta et al. [20], the presence of hypertension (24.95%), malignancy (15.87%), and asthma (14.11%) as comorbidities to PE was reported. While the distribution of comorbid diseases may vary when compared with the outcomes of our study, it could be concluded that malignancy, cardiac diseases, and respiratory system diseases are prominent. This phenomenon may be attributed to similar symptoms presented by cardio-pulmonary diseases and PE, leading clinicians to investigate PE in the differential diagnosis. A noteworthy finding in the current study, unlike other cited studies, is the absence of malignancy accompanying PE in any of the patients. Indeed, although patients in this study did not have a history of active malignancy at the time of PE diagnosis, Li et al. [21] emphasized that PE is an initial sign of cancer. For this reason, the possibility of PE as an early manifestation of cancer in patients should be considered. Thus, in PE-diagnosed patients with risk factors such as advanced age and a family history of malignancy, cancer screening tests are highly recommended.

The D-dimer test, commonly employed in the diagnosis of PE, exhibits a high-negative but a low-positive predictive value [4]. Therefore, a normal D-dimer level eliminates the likelihood of acute PE, while a high D-dimer level is not sufficient for confirming PE [12]. The average D-dimer levels of the patients included in the current study were determined to be 6993.2 ± 7565.7 µg/L (0-500), and a normal D-dimer level was found in 5.4% of the patients. D-dimer values can be measured using different methods in blood samples obtained from patients, and the sensitivity of these methods ranges from 95-99% [22].

Although a negative D-dimer result is considered to exclude the diagnosis of PE, the 5.4% rate of negative results observed in the current study may be attributed to this sensitivity range of the measurement methods. Therefore, even if D-dimer results are normal, in cases where clinical probability is high, applying for advanced imaging studies may be useful for the diagnosis of PE.

In PE, cardiac right ventricular dysfunction is a significant indicator of the prognosis of the disease [4]. Due to its indication of myocardial damage, cardiac troponin value is preferable for identifying high-risk patients [23]. In the current study, the average troponin level was determined to be 0.3 ± 0.6 ng/L (0-0.4), and it was found to be positive in 13.5% of the patients. Similar to the present research, former studies conducted by Douketis et al. [24] and Yalamanchili et al. [25] also reported positive troponin values in patients diagnosed with PE, with the positive patient rates being 13.5% and 16%, respectively.

The limitations of this study include its retrospective design, reliance on data collected from a single center, and its relatively small sample size. Although it has a small sample size, this study has identified atypical symptoms not specific to PE. We believe that our findings will provide guidance for further comprehensive studies.

Conclusion

PE is a remarkable illness highly associated with morbidity and diagnosing the disease is quite challenging. The findings of the present research revealed that in addition to typical clinical findings, PE may present with atypical symptoms that are not specific to the disease. Furthermore, while PE is more frequently observed in the elderly and male population, clinicians should always keep in mind that PE can also occur in low-risk patients due to environmental effects, and women's more frequent use of oral contraceptives. Future studies would focus on comprehensive demographic data of PE by the application of multi-central research in different populations.

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